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EXAMINER	
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1643	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/854,568	BOGOCH, SAMUEL	
	Examiner	Art Unit	
	Stephen L. Rawlings	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2007, has been entered.

1. The amendment filed January 22, 2008, is acknowledged and has been entered. Claim 1 has been amended.

2. The amendment filed October 31, 2007, is acknowledged and has been entered. Claim 14 has been added.

3. Claims 1-4 and 14 are pending in the application and currently under prosecution.

Priority

4. Applicant's claim under 35 U.S.C. §§ 119(e) and/or 120, 121, or 365(c) for benefit of the earlier filing date of Application No. 08/031,562, filed March 16, 1993, which is a continuation-in-part of Application No. 07/744,649, filed August 8, 1991, which is a continuation of Application No. 07/227,621, filed August 3, 1988, which is a continuation of Application No. 06/281,883, filed July 9, 1981, which is a continuation-in-part of Application No. 05/922,799, filed July 7, 1978, and a continuation-in-part of Application No. 06/019,078, filed Mar. 9, 1979, which is a continuation-in-part of Application No. 05/941,940, filed September 13, 1978, which is a continuation of Application No. 05/852,200, filed Nov. 17, 1977, which is a continuation of Application No. 04/621,112, filed October 9, 1975,

which is a continuation-in-part of each of Application No. 04/553,075, filed February 25, 1975, Application No. 04/550,432, filed Feb. 18, 1975, Application No. 04/450,404, filed Mar. 12, 1974, and Application Ser. No. 04/385,451, filed Aug. 3, 1973, is acknowledged.

However, claims 1-4 and 14 do not properly benefit under § 120 by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under § 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). See M.P.E.P. § 201.11.

In addition, claim 14 does not properly benefit under §§ 119 and/or 120 by the earlier filing dates of any prior applications filed before Application No. 06/019,078, filed March 9, 1979, because none of those application describe "Recognin-M", the process by which that substance is made or isolated, or any process by which it is used.

Accordingly, the effective filing date of the claims is deemed the filing date of the instant application, namely May 15, 2001.

Oath/Declaration

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because the date that the declaration was executed is illegible on the copy that has been provided and/or scanned into the electronic file wrapper.

Grounds of Rejection Withdrawn

6. The grounds of rejection set forth in the previous Office action mailed September 24, 2007, have been withdrawn.

Response to Arguments

7. Applicant's arguments with respect to the grounds of rejection of claims 1-4, as set forth in the preceding Office action mailed September 24, 2007, have been considered but are moot in view of the new grounds of rejection.

New Ground of Objection

Specification

8. The specification is objected to because the use of improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

An example of such an improperly demarcated trademark appearing in the specification is Vacutainer™; see, e.g., paragraph [0029] of the published application[1].

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

[1] U.S. Patent Application Publication No. 2002/0045187 A1.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-4 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description'' Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereinafter "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

These guidelines state that rejection of a claim for lack of written description, where the claim recites the language of an original claim should be rare. Nevertheless, these guidelines further state, "the issue of a lack of written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant has possession of the claimed invention" (*Id.* at 1105). The "Guidelines" continue:

> The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art. This problem may arise where an invention is described solely in

> terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process.

With further regard to the proposition that, as *original* claims, the claims themselves provide *in haec verba* support sufficient to satisfy the written description requirement, the Federal Circuit has explained that *in ipsis verbis* support for the claims in the specification does not *per se* establish compliance with the written description requirement:

> Even if a claim is supported by the specification, the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed. The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). *See also:* University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 1892 (CA FC 2004).

Thus, an original claim may provide written description for itself, but it must still be an adequate written description, *which establishes that the inventor was in possession of the invention*.

In this instance, the claims are directed to substances termed “malignin” and “Recognin-M”, which are to be administered to a subject in an amount effective to stimulate an immune response in the subject, and more particularly to elicit the production of an antibody that binds to these substances, so as to inhibit or kill the glioma cells or breast cancer cells in the subject.

The precise, detailed structures of the substance termed “malignin” and “Recognin-M” are not known or disclosed.

Moreover, the specification does not expressly disclose the particularly identifying structural and/or functional features of the substances termed “malignin” and “Recognin-M” to which the claims are drawn, so as to permit the

skilled artisan to immediately envision, recognize or distinguish these substances.

Notably, at paragraph [0034] of the published application, the specification best describes the claimed processes, disclosing that the "Recognin derivative vaccine" can be any product larger, smaller or the same molecular weight, which contains the immunological specificity of malignin, Recognin L or Recognin M.

According to this same disclosure, "Recognin M", as described by Application No. 07/744,649 (now abandoned)[2], can be used.

"Malignin" is further described in this application as the immunogenic fragment of a precursor, namely "Recognin", which is apparently expressed by gliobastoma cells in lieu of the 250 kDa membrane glycoprotein 10B, which is normally expressed in brain cells; see, e.g., paragraph [0013] of the published application. Malignin has a molecular weight of 10 kDa; and the amino acid composition of "malignin", though not the amino acid sequence of the protein, has been disclosed (page 11 of the specification; or paragraph [0020] of the published application).

At paragraph [0020] of the published application, the specification discloses that the preparation of "TARGET reagent" is as previously described in Application No. 07/744,649[3]. Human glioblastoma cells were grown in culture harvested, and homogenized. The homogenate was dialyzed, concentrated by perevaporation, centrifuged, chromatographed, and eluted stepwise with buffered solutions of decreasing pH. The specification indicates that the last eluate contained "malignin".

According to the disclosure in Application No. 07/744,649 this process, when repeated, yielded "malignin" products of varying molecular weights; see, e.g., page 32, Table II, of the prior filed application. The molecular weights of the products yielded ranged rather substantially from 8,900 Daltons to 12,500.

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[2] Application No. 07/744,649 has been incorporated by reference into this application; see, e.g., page 17 of the specification.

[3] Notably, Examples 3-5, beginning at page 28 of the specification of Application No. 07/744,649 describes the processes that were used to isolate "MALIGNIN-Precursor" and then purify "MALIGNIN".

Taken in context, the disclosure of such results suggests that "malignin" is not a single protein, but more probably a plurality of structurally different proteins having varying molecular masses; however, the source of the variability in the masses of these different proteins cannot be known or predicted. The variability might result as a consequence of different degrees of post-translational processing, or perhaps as a consequence of the processes by which these proteins are derived from their precursor in the cancer cells. Another possible source of variation might be the nature of the cancer cells from which the proteins were isolated; it is possible that glioma cells are heterogeneous, perhaps producing structurally different proteins.

In addition, it is further noted that the specification discloses that the vaccine (i.e., the composition comprised of the substances termed “malignin” or “Recognin-M”) can be entirely produced from tissues or cells, or it may be entirely synthetic (paragraph [0034] of the published application); yet, the specification does not describe the materials that are the substances to which the claims are directed, but only a method for isolating those substances.

However, these substances to which the claims are directed cannot be made "synthetically", as might be done *in vitro* or in cell culture using recombinant DNA technology, or using a peptide synthesizer. Since the structure of the materials are unknown (e.g., the amino acid sequences of the polypeptide backbones of these substances are unknown), it would not be possible to use a machine to synthesize the proteins and a nucleic acid molecule encoding a polypeptide having the primary structures of “malignin” and “Recognin-M” cannot be produced or used in the synthesis.

In addition, since the specification describes the substances termed “malignin” and “Recognin-M” as glycoproteins (i.e., conjugated proteins having a carbohydrate component), or derivatives thereof, having a molecular mass of about 10 kDa (see, e.g., paragraph [0013] of the published application), it is aptly noted that the antigenic determinants of which the substances are comprised, which elicit antibodies capable of inhibiting the growth of the cancer cells, may

not be contained by the peptide backbone. Instead it is just as probable that the immunogenicity of the substances is an attribute of the carbohydrate moieties or the junctions of these moieties and the peptide. If that is the case, synthesizing a peptide having the amino acid sequence of the substances termed "malignin" and "Recognin-M" would not necessarily produce an immunogen capable of eliciting the requisite immune response in the subject, which is directed against the cancer cells.

Therefore, the specification would at best provide an adequate written description of the products produced by processes that are clearly and particularly described in this application, as opposed to any product that might be deemed immunologically the same or equivalent to those products that were isolated and purified by those processes.

"[G]eneralized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

In this instance, there is no language that adequately describes with the requisite clarity and particularity the substances termed "malignin" and "Recognin-M" to which the claims are directed, which can be used in practicing the claimed process to achieve the claimed therapeutic effect. A description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

Moreover, the Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568). As discussed, because the specific nature and substance of "malignin" and "Recognin-M", which gives rise to the desired immune response in the subject is unknown, there is in fact such unpredictability.

For example, even if a 10 kDa protein resembling "malignin" in amino acid composition were known, it could not be predicted whether that protein is capable of eliciting an anti-glioma immune response of sufficient magnitude and/or specificity to inhibit the growth of those cancer cells.

Importantly, it is not the amino acid composition of an antigenic protein that gives rise to a specific immune response against that protein; rather it is the protein's three-dimensional structure, determined in part by its amino acid sequence and the conformation assumed by the molecule in space.

Then, since the protein is apparently derived from a glycoprotein precursor, it is just as likely that the specific immune response elicited by the protein, which is effective to inhibit the growth of cancer cells, is attributable to the structure of the carbohydrate moieties of which it is comprised.

There is simply no way of meaningfully predicting whether any 10 kDa glycoprotein having an amino acid composition resembling "malignin" might be capable of eliciting the requisite immune response in the subject.

While the written description requirement can by satisfied without an actual reduction to practice, the disclosure of the processes by which products termed “malignin” and “Recognin-M” were isolated and purified by Applicant is not sufficient to satisfy that requirement, unless the products to which the claims are directed are necessarily products produced by those processes, since otherwise there is simply no way of knowing whether either one of the products is at hand.

Furthermore, merely having disclosed the recognized functional attribute of the substances isolated and purified by the disclosed processes, rather a recitation of their precise structures does not satisfy the written description requirement.

The Federal Circuit has decided that a generic statement that defines a genus of substances by *only* their functional activity, i.e., the ability to elicit an immune response in a subject, so as to achieve therapeutic effect, does not provide an adequate written description of the genus. See *The Reagents of the*

University of California v. Eli Lilly, 43 USPQ2d 1398 (CAFC 1997). The Court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

Although *Lilly* related to claims drawn to genetic material, the statute applies to all types of inventions. "Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods". *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1894 (CAFC 2004). The claimed method depends upon knowing those substances to which the claims are directed, namely those substance termed "malignin" and "Recognin-M", which can be used to achieve therapeutic effect in treating glioma or breast cancer in subjects in accordance with the claims; without such substances, it is impossible to practice the invention.

Although the skilled artisan could potentially identify substances, perhaps having the same molecular weight or the same amino acid composition as the product isolated and purified by processes disclosed in this application, which might be used in practicing the claimed inventions to achieve the claimed effects, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

Finally, Guidelines states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims apparently encompass pluralities of substances having the ability to elicit a specific immune response in a subject, so as to inhibit the growth of cancer cells, but which otherwise vary both structurally and functionally, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. In this instance, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; Applicant has not shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; and Applicant has not described distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed.

For all of the above reasons, it is submitted that the specification would not reasonably convey to the skilled artisan that Applicant had possession of the

claimed invention at the time the application was filed, so as to satisfy the written description requirement set forth under 35 U.S.C. § 112, first paragraph.

11. Claims 1-4 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** a process for inhibiting the growth or proliferation of glioma cells in a subject, said process comprising administering to said subject a composition comprising an amount of malignin effective to stimulate the immune system of the subject, so as to cause the production and release of an anti-malignin antibody, which is binds to and inhibits glioma cells in the subject, wherein said malignin is that substance that is produced by the process described in Examples 3-5, beginning at page 28 of the specification of Application No. 07/744,649, which substance is characterized as having a molecular weight of approximately 10,000 Daltons and the amino acid composition set forth at page 11 of this application, **and for using** a process for killing breast cancer cells in a subject, said process comprising administering to said subject a composition comprising an amount of Recognin-M effective to stimulate the immune system of the subject, so as to cause the production and release of an anti-Recognin-M antibody, which is binds to and inhibits glioma cells in the subject, wherein said Recognin-M is that substance that is produced by the process described in Examples 5B, beginning at page 34 of the specification of Application No. 07/744,649, which substance is characterized as having a molecular weight of approximately 10,000 Daltons and the amino acid composition set forth at page 36 of Application No. 07/744,649, **does not reasonably provide enablement for using** a process for inhibiting the growth or proliferation of glioma cells in a subject, said process comprising administering to said subject a composition comprising an amount of malignin effective to stimulate the immune system of the subject, so as to cause the production and release of an anti-malignin antibody, which is binds to and inhibits glioma cells in the subject, **or for using** a process for killing breast cancer cells in a subject, said process comprising administering to said subject a composition comprising

an amount of Recognin-M effective to stimulate the immune system of the subject, so as to cause the production and release of an anti-Recognin-M antibody, which is binds to and kills breast cancer cells in the subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

M.P.E.P. § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

As explained in the above rejection of the claims, as failing to satisfy the written description requirement, the specification, as filed, is only sufficient

enabling of the isolation and purification of the substance termed “malignin”, which is produced by the process described in Examples 3-5, beginning at page 28 of the specification of Application No. 07/744,649, which substance is characterized as having a molecular weight of approximately 10,000 Daltons and the amino acid composition set forth at page 11 of this application.

The specification, as filed, would not reasonably enable the skilled artisan to make or synthesize by any other means the substance termed "malignin" to which the claims are directed, which substance is effective to elicit in a subject an immune response that leads to the production of anti-malignin antibodies that bind to and inhibit the growth and/or proliferation of glioma cells in the subject without undue and/or unreasonable experimentation since the immunogenic and therapeutic properties of any other substance, or the specificity and/or therapeutic effects of antibodies produced in response to immunization thereby, cannot be known or predicted.

In addition, as also explained in the above rejection of the claims, as failing to satisfy the written description requirement, the specification, as filed, is only sufficient enabling of the isolation and purification of the substance termed “Recognin-M”, which is produced by the process described in Examples 5B, beginning at page 34 of the specification of Application No. 07/744,649, which substance is characterized as having a molecular weight of approximately 10,000 Daltons and the amino acid composition set forth at page 36 of Application No. 07/744,649.

The specification, as filed, would not reasonably enable the skilled artisan to make or synthesize by any other means the substance termed " Recognin-M " to which the claims are directed, which substance is effective to elicit in a subject an immune response that leads to the production of anti-Recognin-M antibodies that bind to and kill breast cancer cells in the subject without undue and/or unreasonable experimentation since the immunogenic and therapeutic properties of any other substance, or the specificity and/or therapeutic effects of antibodies produced in response to immunization thereby, cannot be known or predicted.

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enabled the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bogoch et al. (1984) (of record; cited by Applicant as Reference #6) and Bogoch et al. (*Prog. Clin. Biol. Res.* 1980; **39**: 407-424) (of record; cited by Applicant).

Bogoch et al. (1980) teaches the survival rate of cancer patients with low level of serum anti-malignin antibody is poorer, as compared to cancer patients

with relatively high level of serum anti-malignin antibody; see entire document (e.g., page 422). Bogoch et al. teaches the antibody thus seems to be beneficial (page 422). Moreover, Bogoch et al. teaches anti-malignin antibody is cytototoxic to malignant glial cells *in vitro* (page 422). Finally, Bogoch et al. teaches the antibody preferentially binds to glioma cells *in vivo* (page 422).

Bogoch et al. (1984) suggests that anti-malignin antibody has therapeutic properties; see entire document (e.g., page 746). Bogoch et al. further suggests that stimulating the production of anti-malignin antibody, so as to replace the antibody produced in cancer patients, which is somehow defunct, or to increase the concentration of the antibody in patient, by active or passive immunotherapy will be clinically effective against cancer (page 746).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have administered to a subject an amount of a composition comprising malignin, which is effective to stimulate the immune system of the subject, so as to produce and release anti-malignin antibody into the subject's serum, because Bogoch et al. (1980) suggests that doing so to stimulate the production of anti-malignin antibody, and to thereby replace the antibody produced in cancer patients, which is somehow defunct, or to increase the concentration of the antibody in patient, will be clinically effective against cancer. One of ordinary skill in the art at the time the invention was made would have been motivated to have done so in order to treat a glioma in the subject. One of ordinary skill in the art at the time the invention would have had a reasonable expectation of successfully treating glioma by doing so because Bogoch et al. (1984) teaches the survival rate of cancer patients with low level of serum anti-malignin antibody is poorer, as compared to cancer patients with relatively high level of serum anti-malignin antibody, the antibody preferentially binds to glioma cells *in vivo*, and it is cytototoxic to glioma cells.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16, 20, 22, and 24-26 of U.S. Patent No. 5,866,690 A. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

In responding to the restriction and election requirement set forth in the Office action mailed September 20, 2004, Applicant elected the invention of Group I, claims 1-5, drawn to a process for stimulating the immune system of a subject to produce and release anti-malignin antibody, said process comprising administering to the subject an effective amount of a first dosage of a composition comprising malignin, recognin M, Recognin L or a peptide having the immunological specificity thereof.

At present claim 1 is directed to a method for inhibiting glioma cancer cells in a subject wherein said glioma cancer cells express malignin, said method comprising administering to said subject an effective amount of a first dosage of a composition comprising malignin, wherein said administration of said dosage stimulates the immune system of said subject to produce and release anti-malignin antibody that binds and inhibits said glioma cancer cells.

Claims 1-16, 20, 22, and 24-26 of U.S. Patent No. 5,866,690 A is directed to a process for producing anti-malignin antibody in a subject, said process comprising selecting a subpopulation of human lymphocytes producing said antibody, culturing the isolated lymphocytes and/or stimulating the lymphocytes to proliferate and produce the antibody, and optionally isolating the antibody; see, e.g., claim 16.

Although the claims of the patent are not expressly directed to a process comprising an active step of administering to a subject an amount of a composition comprising malignin, which is effective to stimulate the immune system of said subject to produce and release anti-malignin antibody, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have done so because the art of eliciting the production of antibodies that specifically bind to an antigen of interest by administering to a subject a composition comprising that antigen was well established. In addition, claims 1-16, 20, 22, and 24-26 of U.S. Patent No. 5,866,690 A make evident the fact that malignin is a cancer cell associated antigen in that the anti-malignin antibody is an "anti-cancer recognin antibody", as in accordance with claims 1

and 16. Furthermore, since according to claim 20, the isolated antibody is conjugated to a chemotherapeutic agent, it is evident that the antibody may be used to target cancer cells expressing malignin, namely those cancer cells from which the antigen was isolated (i.e., glioma cells).

Then, with regard to the instant claims, although the invention is now intended for use in inhibiting glioma cells expressing malignin in a subject, the claims do not recite a limitation requiring that the subject have a glioma; inasmuch as the subject need not have a glioma, it is submitted that the process that would have been obvious to one of ordinary skill in the art at the time the invention was made in light of claims 1-16, 20, 22, and 24-26 of U.S. Patent No. 5,866,690 A is a process that is materially and manipulatively indistinguishable from the active process of the claimed invention.

Accordingly, the claimed inventions are so substantially similar that for the most part, the claimed subject matter of the patent anticipates the claimed subject matter of the instant application, and any minor differences in the subject matter claimed in the instant application would be seen as an obvious variation of the subject matter claimed in the patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to have practiced the process, as claimed in this application, in view of claims 1-16, 20, 22, and 24-26 of U.S. Patent No. 5,866,690 A in order to elicit an immune response in a subject, so as to produce in the subject an antibody that specifically binds to malignin, which as evidenced by the patent is an antibody having a specific and substantial, credible, and/or well established utility.

With regard to claim 2, although not expressly suggested by the prior art, administering a dose of approximately 1 mg of malignin would not have been unexpectedly low or high, given that the objective of the administering that dose of malignin must stimulate an immune response in the subject. Then, with regard to claims 3 and 4, it was, at the time the invention was made, conventional to boost the immune response by repeated immunizations; although the claims are

directed to processes comprising administering a second dose ten days after the first, and then a third dose ten after the second, and the prior art does not expressly teach or suggest that such a schedule be applied, it is nevertheless a common objective in the art to establish a dose and a schedule that is both safe and effective, so as achieve optimal therapeutic effect and maximal benefit. See *In re Boesch*, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980) ("[D]iscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." (citations omitted)). See *In re Peterson*, 65 USPQ2d 1379 1382 (CA FC 2003): "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." It is therefore submitted that the limitations set forth in claims 2-4 should not be viewed as requiring any unobvious variation of the process of claim 1, which would have been obvious in light of the express disclosures by the prior art.

Conclusion

17. No claim is allowed.

18. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Bogoch et al. (*Neurochem. Res.* 1979; **4** (4); 465-472) describes the isolation and purification of Recognin-M from mammary MCF-7 carcinoma cells. Bogoch (*In* Current Trends in Sphingolipidoses and Applied Disorders. Eds. Volk et al; 1976; New York: Plenum Press; pp. 555-566) teaches anti-malignin antibody is cytototoxic to malignant glial cells.

19. Applicant is advised that it appears that any patent that issues from this application, were this application deemed to benefit from the filing date(s) of the prior filed applications, as presently sought by Applicant, would be unenforceable, as the patent term will have expired immediately following its

issue. The expiration date of the patent term will be determined from the earliest effective U.S. filing date of this application.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephen L. Rawlings/
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Primary Examiner, Art Unit 1643

slr
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